

**REMARKS**

Claims 1-25 were pending in the application upon issuance of the Office Action. According to the foregoing amendments, claims 2, 5-11, 13-17, 19-21, 24 and 25 have been cancelled, claims 1, 4, 12, 18, and 22 have been amended, and new claims 26-48 have been added. Following entry of this amendment, claims 1, 3, 4, 12, 18, 22, 23, and 26-48 will be pending in the instant application.

Support for the amendments to the claims can found throughout the specification and in the claims as originally filed. Specifically, support for the amendments to claims 1, 12, 18 and 22, and new claims 26-38, can be found in the specification at least at page 29, lines 18-21; page 13, lines 7-13; page 33, lines 12-17; and page 36, lines 29-31. Support for the amendments to claims 4, 18, 19 and 22, and new claim 27, can be found in the specification at least at page 3, lines 27-29. Support for new claims 39-48 can be found in the specification at least at page 39, line 29 to page 41, line 29.

The specification has been amended to update the status of referenced non-provisional U.S. Patent Applications. In addition, the specification has been amended to replace the notation "Attorney Docket No." with the serial numbers of referenced U.S. Patent Applications, and to provide the generic terminology for any compounds associated with trademarks.

No new matter has been added by the foregoing amendments. Applicants request that the amendments to the claims and specification be entered. The foregoing claim amendments should in no way be construed as acquiescence to any of the Examiner's rejections and were made solely to expedite prosecution of the present application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

***Interview***

Applicants wish to thank the Examiner for the courtesy of a personal interview on March 6, 2008 conducted at the USPTO with Applicants' attorneys Elizabeth Hanley and Cristin Cowles. During the interview, amendments to the claims were discussed. In particular, it was pointed out that the amended claims in the instant Amendment and Response were not rejected under 35 USC § 112, 1<sup>st</sup> paragraph in the Office Action dated September 24, 2007 with respect to CDR sequences. It was also

discussed that the limitations of the amended claims (submitted herewith) were not taught or suggested by the combination of references cited under 35 USC § 103.

***Restriction Requirement***

The Examiner has required restriction to one of the following inventions under 35 U.S.C. 121:

I. Claims 1-23, drawn to a method of treating a subject suffering from spondyloarthropathy comprising administering a human antibody that binds TNF $\alpha$ , classified in class 424, subclass 145.1.

II. Claims 24-25, drawn to a kit comprising a human TNF $\alpha$  antibody, classified in class 530, subclass 388.23.

Applicants hereby affirm the election of Group I and the species “psoriatic arthritis.” Claims 1, 3, 4, 12, 18, 22, 23 and 26-48 read on the elected invention.

***Objections to the Specification***

The Examiner has indicated that the specification should be updated to include the current status of non-provisional U.S. Patent Applications referenced therein. The status of the non-provisional U.S. Patent Applications has been updated as requested. The specification has additionally been amended to replace the notation “Attorney Docket No.” with the serial numbers of referenced U.S. Patent Applications, and to provide the generic terminology for any compounds associated with trademarks. The title of the application will be amended in accordance with the Examiner’s recommendation upon allowance of the claims.

***Claim Objections***

The Examiner has objected to claim 15 as improperly depending from withdrawn claim 13. Applicants have canceled claim 15, thereby obviating this objection.

***Rejection of Claims 4, 15, 18, 20, 22 and 23 Under 35 USC § 112, Second Paragraph***

The Examiner has rejected claims 4, 15, 18, 20, 22 and 23 under 35 U.S.C. § 112, second paragraph for recitation of the term “D2E7”. The Examiner alleges that recitation of “D2E7” in the claims is indefinite and states that the term is “merely a laboratory designation.” Applicants respectfully traverse this rejection on the grounds that the term “D2E7” as used in the claims is clear and definite to one of ordinary skill in the art, as the term refers specifically to the anti-TNF $\alpha$  antibody sold under the generic name adalimumab and the brand name HUMIRA<sup>®</sup>. Notwithstanding the foregoing, Applicants have amended claims 4, 18, 22 and 23 to recite “adalimumab,” and have canceled claims 15 and 20, thereby rendering the rejection moot. These amendments were made solely in the interest of expediting examination, and are in no way an acquiescence of the validity of the Examiner’s rejection.

Examiner has further rejected claims 4 and 15 for recitation of the phrase “[the] antigen-binding fragment thereof, is D2E7.” The Examiner suggests that “while an antigen-binding fragment can be produced from antibody D2E7, one of skill in the art would not be reasonably apprised of the metes and bounds of D2E7 being an antibody and an antigen-binding fragment thereof.” Solely in the interest of expediting examination and in no way acquiescing to the validity of the Examiner’s rejection, Applicants have canceled claim 15, and have amended claim 4 to recite “wherein the antibody is adalimumab, or an antigen-binding fragment thereof,” thereby rendering the foregoing rejection moot.

***Rejection of Claims 2, 4, 6, 15, 18, 20, 22 and 23 Under 35 USC § 112, First Paragraph***

***I. Rejection of Claims 4, 15, 18, 20, 22 and 23 Under 35 USC § 112, First Paragraph***

Claims 4, 15, 18, 20, 22 and 23 have been rejected under 35 U.S.C § 112, first paragraph for allegedly failing to comply with enablement requirement. Specifically, the Examiner asserts that the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; and (2) reproducible from the written description.

Applicants respectfully traverse this rejection. Applicants have disclosed, and one of ordinary skill in the art will recognize, that D2E7 is also referred to as

HUMIRA<sup>®</sup> and adalimumab (see also page 3, lines 27-29 of the specification).

HUMIRA<sup>®</sup> is well known in the art and is readily available to the public.

Furthermore, Applicants have provided sufficient guidance with respect to the amino acid sequence of the variable heavy and variable light chains of D2E7. One or ordinary skill in the art can easily make D2E7 using recombinant molecular biological techniques (see, for example, page 21, line 5 to page 27, line 26 of the specification). Applicants respectfully note that a deposit of the antibody D2E7, or a cell line that produces the antibody D2E7, is not required for one of ordinary skill in the art to practice Applicants' claimed method as the antibody is publicly available. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection of claims 4, 18, 22 and 23 under 35 U.S.C. § 112, first paragraph. Applicants note that claims 15 and 20 have been canceled, thereby rendering rejection of these claims moot.

## II. *Rejection of Claims 2 and 6 Under 35 USC § 112, First Paragraph*

Claims 2 and 6 have been rejected under 35 U.S.C. § 112, first paragraph for allegedly failing to comply with the enablement requirement. The Examiner suggests that the instant specification lacks a sufficient enabling description of molecules containing at least one, but fewer than all, of the CDRs described in SEQ ID NOs: 3-8.

Applicants respectfully traverse this rejection. Applicants assert that not all of the CDRs of the antigen binding site may be necessary (or even utilized) in binding a specific antigen, and that functional antibody fragments comprising fewer than all 6 CDRs are well known by practitioners skilled in the art. Notwithstanding the foregoing, and in the interest of expediting examination, Applicants have canceled claims 2 and 6, thereby rendering rejection of these claims moot. Applicants submit that the cancellation of claims 2 and 6 in no way is an acquiescence to the Examiner's rejection. Applicants preserve the right to pursue the subject matter of claims 2 and 6 in a future continuation or divisional application.

## ***Rejection of Claims 1-4, 6, 12, 14-15, 18, 20, 22 and 23 Under 35 USC § 103(a)***

Claims 1-4, 6, 12, 14-15, 18, 20, 22 and 23 have been rejected under 35 U.S.C. § 103(a) as being *prima facie* obvious over either (1) Ogilvie *et al.* (British Journal of Dermatology, 144(3):587-589, March 2001) in view of Salfeld *et al.* (WO 97/29131)

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and Smith *et al.* (Arthritis Rheum. 23(8):961-962, August 1980) or (2) Ogilvie *et al.* in view of Salfeld *et al.* (U.S. Patent No. 6,509,015) and Smith *et al.* (Applicants note that claims 2, 6, 14, 15 and 20 have been canceled, thereby rendering rejection of these claims moot). Specifically, the Examiner alleges that:

One of ordinary skill in the art would have been motivated to modify the method of Ogilvie *et al.* and administer the human anti-human TNF $\alpha$  antibodies and antigen-binding fragments thereof of Salfeld *et al.* in combination with ibuprofen in order to avoid any unwanted immune reaction in human patients due to the presence of murine sequences in the chimeric anti-TNF $\alpha$  antibody of Ogilvie *et al.* and reduce pain and joint swelling in psoriatic arthritis patients. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. (Office Action at page 19)

Applicants respectfully traverse this rejection. Amended claims 1, 3, 12, and 22 (as well as new claims 26 and 27) require *biweekly, subcutaneous administration* of a *unit dosage form* comprising *10-150 mg* of a human anti-TNF $\alpha$  antibody, or an antigen binding fragment thereof. In addition, amended claim 18 requires *biweekly, subcutaneous administration* of a unit dosage form comprising about *40 mg of adalimumab*.

“To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.” (See MPEP § 2143; emphasis added).

Ogilvie *et al.* is the primary reference relied upon by the Examiner for teaching methods of treating psoriatic arthritis. Salfeld *et al.* was cited by the Examiner as a secondary reference, and is relied up for teaching a human TNF $\alpha$  antibody. Applicants submit that Ogilvie *et al.* fails to teach or suggest the method of treating psoriatic arthritis described in the amended claims. Ogilvie *et al.* describe six patients who received three infusions of the chimeric TNF $\alpha$  antibody infliximab at a weight-based dose of 5 mg/kg at weeks 0, 2 and 6. Ogilvie *et al.* fail to teach or suggest the claimed methods of treating psoriatic arthritis, or inhibiting

TNF $\alpha$  activity in a subject having PsA, comprising biweekly, subcutaneous administration of a unit dosage form comprising 10-150 mg of a TNF $\alpha$  antibody.

Applicants respectfully submit that Ogilvie *et al.* does not teach each and every element of the invention, either alone or in combination with Salfeld *et al.* and/or Smith *et al.* In view of the required elements of amended claims 1, 3, 12, 18 and 22, and new claims 26 and 27, Ogilvie *et al.*, as the primary reference, fails to make up for the deficiencies of either Salfeld *et al.* and/or Smith *et al.* Accordingly, Applicants respectfully request that the rejection of the pending claims under 35 U.S.C. § 103 be reconsidered and withdrawn.

***Rejection of Claims 1-4, 6, 12, 14, 15, 18, 20, 22 and 23 On Grounds of Non-Statutory Obviousness-Type Double Patenting***

The Examiner has rejected claims 1-4, 6, 12, 14, 15, 18, 20, 22 and 23 on grounds of non-statutory obviousness-type double patenting as allegedly being unpatentable over claims 1-7, 36-39 and 69 of U.S. Patent 6,509,015 B1 (Salfeld *et al.*) in view of Ogilvie *et al.* and Smith *et al.* The Examiner suggests that claims 1-4, 6, 12, 14, 15, 18, 20, 22 and 23 are not patentably distinct from claims 1-7, 36-39 and 69 of Salfeld *et al.* because “it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the method of...U.S. Patent No. 6,509,015 B1 comprising administering the human anti-human TNF $\alpha$  antibodies for the treatment of psoriatic arthritis and optionally administer the human TNF $\alpha$  antibodies in combination with ibuprofen in view of the teachings of Ogilvie *et al.* and Smith *et al.*” Applicants note that the pending claims all require *biweekly, subcutaneous administration* of an anti-TNF $\alpha$  antibody, or antigen binding portion thereof, *as a unit dosage form*. The Examiner relies on Ogilvie *et al.* and Smith *et al.* to make up for the deficiencies of claims 1-7, 36-39 and 69 of Salfeld *et al.* Applicants respectfully submit that in view of the fact that Ogilvie *et al.* and Smith *et al.* do not teach or suggest all of the limitations of the claims, as described above, Ogilvie *et al.* and Smith *et al.* fail to make up for the deficiencies of Salfeld *et al.* As such, Applicants respectfully request that the rejection of claims 1-4, 6, 12, 14, 15, 18, 20, 22 and 23 on the ground of nonstatutory obviousness-type double patenting be withdrawn.

***Provisional Rejection of Claims 1-4, 6, 12, 14, 15, 18, 20, 22 and 23 On Grounds of Non-Statutory Obviousness-Type Double Patenting***

The Examiner has provisionally rejected claims 1-4, 6, 12, 14, 15, 18, 20, 22 and 23 as being unpatentable on the ground of nonstatutory obviousness-type double patenting over claims 1, 4-8 and 10-14 of Applicants' copending Application No. 11/435,844 in view of Ogilvie *et al.* and Smith *et al.* Claims 1-4, 6, 12, 14, 15, 18, 20, 22 and 23 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-23, 73-84 and 86-99 of Applicants' copending Application No. 10/163,657 in view of Ogilvie *et al.* and Smith *et al.* Claims 1-4, 6, 12, 14, 15, 18, 20, 22 and 23 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 15, 19, 56, 66, 77, and 87 of Applicants' copending Application No. 11/233,252 in view of Ogilvie *et al.* and Smith *et al.* Claims 1-4, 6, 12, 14, 15, 18, 20, 22 and 23 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 1, 2 and 4-14 of Applicants' copending Application No. 10/622,932 in view of Ogilvie *et al.* and Smith *et al.* Claims 1-4, 6, 12, 14, 15, 18, 20, 22 and 23 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-11 of Applicants' copending Application No. 10/623,075 in view of Ogilvie *et al.* and Smith *et al.* Claims 1-4, 6, 12, 14, 15, 18, 20, 22 and 23 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 1, 3-14 and 16 of Applicants' copending Application No. 10/623,318 in view of Ogilvie *et al.* and Smith *et al.*

Applicants note that these rejections are provisional in nature and respectfully submit that they will be further addressed when appropriate, *i.e.*, when the nonstatutory obviousness-type double patenting rejection is the only rejection remaining in the later-filed application (MPEP § 804 I.B.).

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If a telephone conversation with Applicant's agent would help expedite the prosecution of the above-identified application, the Examiner is urged to call Applicant's agent at (617) 227-7400.

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Respectfully submitted,

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